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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,519	01/16/2004	Charles R. Cantor	701586-53651	7045
50607	7590	04/12/2006	EXAMINER	
RONALD I. EISENSTEIN 100 SUMMER STREET NIXON PEABODY LLP BOSTON, MA 02110			KAPUSHOC, STEPHEN THOMAS	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,519	CANTOR ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-18 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 24 May 2004 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/7/05 11/21/05</u> . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 4/7/05 and 11/21/05 have been considered by the examiner. The citations designated as C2-C11 and C13-C30 on the IDS of 11/21/05 have been lined through because they are duplicated from the IDS of 4/7/05. The citation designated as C24 on the IDS of 4/7/05 has been lined through because it is a duplicate of C11 on the same IDS.

Specification

2. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (for example see paragraphs 51 and 52 on page 14). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

3. Claim 17 is objected to because of the following informalities:

Step (e) of claim 17 recites the phrase 'at least one polymorphic markers', in which there is not agreement between the singular 'one polymorphic' and the plural 'markers'.

Appropriate correction is required.

4. Claim 7 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim 7 has not been further treated on the merits.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 8-11 are unclear over the recitation of the phrase 'the diluted single nucleotide dilution' in claims 1 and 9 (each step (b)) because there is no antecedent basis in the claims for a single nucleotide dilution. Additionally, it is unclear how a haplotype can be detected in a target that is a single nucleotide.

Claims 4, 5, and 6 are unclear over the recitation of the phrase 'the polymorphism' because the base claim (claim 1) from which the rejected claims depend recites only multiple polymorphisms, thus it is unclear as to which of the multiple polymorphic markers is 'the polymorphism'.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruano et al (1990) (as cited in the IDS).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule.

Ruano et al teaches that a nucleic acid sample is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a) of claim 1. Relevant to step (b), the reference further teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification).

Additionally relevant to step (b), Ruano et al teaches amplification with another different primer pair (GR5 and GR6) (Fig 1) designed to amplify a region comprising a single base substitution polymorphism at a *TaqI* site in addition to the three previously mentioned polymorphic sites. Further relevant to step (b), the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion). Relevant to step (c), Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by southern hybridization (Fig 4) and restriction digestion (Fig 3).

Relevant to step (d), the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products).

Regarding claim 2, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) of claim 1. The reference specifically teaches that for ‘Person B’ the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Regarding claims 4-6, Ruano et al teaches the analysis of a haplotype comprising polymorphic sites that are single nucleotide polymorphisms and a dinucleotide insertion/deletion (Fig 1).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 3 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (as cited in the IDS) in view of Drysdale et al (2000) (as cited in the IDS).

Ruano et al teaches a method for the determination of haplotypes amplified from a single DNA molecule, and the analysis of multiple replica genotypes.

Ruano et al teaches that a nucleic acid sample is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a) of claims 1 and 9, from which the rejected claim depend. Relevant to step (b) of claims 1 and 9, the reference further teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification). Additionally relevant to step (b) of claims 1 and 9, Ruano et al teaches amplification with another different primer pair (GR5 and GR6) (Fig 1) designed to amplify a region comprising a single base substitution polymorphism at a *TaqI* site in addition to the three previously mentioned polymorphic sites. Further relevant to step (b) of claims 1 and 9, the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion). Relevant to step (c) of claims 1 and 9, Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by southern hybridization (Fig 4) and restriction digestion (Fig 3). Relevant to step (d) of claims 1 and 9, the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products).

Ruano et al further teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), relevant to claim 2 and claim 10, and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) of claims 1 and 9. The reference specifically teaches that for ‘Person B’ the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Regarding claim 11, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., Ins.43-45).

Ruano does not teach the comparison of a deduced haplotype with a haplotype from a control or a database of haplotypes to determine association of the haplotype with a biological trait, as required for claim 3, and step (e) of claim 9.

Drysdale et al teaches the use of β_2 -adrenergic (β_2 AR) receptor haplotypes in the prediction of response to albuterol (p.10486, left col., Ins.6-8), which is a biological trait.

Regarding claim 3 and step (e) of claim 9 Drysdale et al teaches a collection of (β_2 AR) haplotype pairs found in a cohort of asthmatics (p.10486, right col., Ins.3-10; Table 2) (thus a database of haplotypes), as well as the association of the five most common haplotype pairs with patient response to albuterol (Fig.3; p.10487, left col., Ins.1-25). The reference further teaches comparing a haplotype to the database of

haplotypes and association data to determine association of the haplotype with a biological trait (Fig.3; p.10487, left col., Ins.25-30).

It would have been *prima facie* obvious to one of skill in the art at the time the invention was made to have used the haplotype determination methods of Ruano et al for the predictive analysis of haplotypes as taught by Drysdale et al. One would have been motivated to do so based on the assertion of Drysdale et al that haplotypes are more predictive of phenotype, and that individual SNPs may have poor predictive power as pharmacogenetic loci (p.10488, right col., Ins.13-17). With specific regard to claim 11, it would be obvious to create and analyze numerous replicas, including producing 12-18 replicas, to increase the accuracy of the analysis. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., Ins.43-45).

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (as cited in the IDS).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule, relevant to claims 1 and 2, from which the rejected claim depends. The reference teaches that a nucleic acid sample is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a) of claim 1. Relevant to step (b), the reference further teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region

comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification).

Additionally relevant to step (b), Ruano et al teaches amplification with another different primer pair (GR5 and GR6) (Fig 1) designed to amplify a region comprising a single base substitution polymorphism at a *TaqI* site in addition to the three previously mentioned polymorphic sites. Further relevant to step (b), the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion). Relevant to step (c), Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by southern hybridization (Fig 4) and restriction digestion (Fig 3). Relevant to step (d), the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products). Relevant to claim 2, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) of claim 1. The reference specifically teaches that for 'Person B' the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Ruano et al does not specifically teach the analysis of 12-18 genotype replicas.

Regarding claim 8, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., Ins.43-45).

It would have been *prima facie* obvious to one of skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al to produce and analyze 12-18 replicas. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., Ins.43-45).

12. Claims 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al 1990 (as cited in the IDS) in view of Rein et al (1998).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule. The reference teaches that a nucleic acid sample is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3). The reference further teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification). Additionally, Ruano et al teaches amplification with another different primer pair (GR5 and GR6) (Fig 1) designed to amplify a region comprising a single base substitution polymorphism at a *TaqI* site in

addition to the three previously mentioned polymorphic sites. Furthermore, the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion). Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by southern hybridization (Fig 4) and restriction digestion (Fig 3). The reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products). Thus, Ruano teaches steps (b)-(e) of claim 12, and steps (b)-(d) of claim 17. With particular regard to step (c) of claim 17, Ruano et al teaches the amplification of samples diluted to a single molecule concentration, as well as amplification of more concentrated samples (Fig 3; p.6297 – Standard PCR).

Regarding claim 13, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (b)-(d) of claim 12. The reference specifically teaches that for 'Person B' the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Regarding claim 14, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., Ins.43-45).

Regarding claim 18, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (b)-(d) of claim 17. The reference specifically teaches that for ‘Person B’ the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Ruano et al does not teach an analysis of a nucleic acid sample that contains epigenetically modified nucleotides by specifically treating modified nucleotides (relevant to step (a) of claim 12) or digestion of a nucleic acid sample with a methylation sensitive restriction enzyme (relevant to step (a) of claim 17).

Rein et al teaches method for the identification of 5-methylcytosine and related modifications in DNA genomes (Table 1; p.2255, right col., first full paragraph).

Regarding claim 12, Rein et al teaches methods for analysis of 5-methylcytosine (m^5C , which is a modified nucleotide) by treating genomic DNA with a composition that differentially affects epigenetically modified nucleotides by converting non-methylated C to U, and not altering m^5C (p.2258 – Differential base modification by bisulfite), relevant to step (a) of claim 12, thus effectively creating polymorphisms (the content at a given nucleotide position can be a C if the position is methylated, or U (which behaves similar to a T in subsequent base pairing processes) if the position is nonmethylated) based on the epigenetic methylation modification (Fig 2).

Regarding claim 15, Rein et al teaches the analysis of 5-methylcytosine (m^5C), which is a methylated nucleotide (p.2258 – Differential base modification by bisulfite).

Regarding claim 16, Rein et al teaches the use of bisulfite for the treatment of a nucleic acid sample (p.2258 – Differential base modification by bisulfite; Table 1; p.2255, right col., ln.25).

Regarding claim 17, Rein et al teaches methods for analysis of methylated bases at specific DNA sites use modification-sensitive restriction endonucleases (Table 1; p.2257 - Modification-sensitive restriction endonucleases (MSREs); Fig 1). Relevant to step (a) of claim 17, the reference teaches the digestion of a sample with restriction enzymes that are sensitive to base modification (i.e. will not digest methylated sites) and restriction enzymes that require base modification (i.e. will only digest methylated sites) (p.2257, left col., Ins.14-24; Fig 1). Relevant to step (e) of claim 17, Rein et al teaches the analysis of the methylation dependent digestion of a sample by Southern analysis and PCR amplification (Fig 1; p.2258, left col., Ins.15).

It would have been *prima facie* obvious to one of skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al so as to have included the methylation analysis methods of Rein et al. One would have bee motivated to do so because Rein et al teaches that m^5C in the genomes of eukaryotic cells plays a role in a variety of processes (p.2255, left col., first paragraph of introduction). One would have been motivated to use the bisulfite treatment of Rein et al (relevant to claims 12-16) because Rein et al teaches that such methods are highly sensitive, are amenable to rapid genomic sequencing, and provide positive display of

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m^5C (Table 1). One would have been motivated to use the MSRE method of Rein et al (relevant to claim 17 and 18) because Rein et al teaches that such methods provide a rapid analysis of large DNA regions, and are highly sensitive. With particular regard to step (e) of claim 17, the combination of the restriction enzyme digestion methods of Rein et al (as summarized in Fig 1 of Rein et al) and the haplotype determination methods of Ruano et al would create a method where, for example, the DNA sample amplified by GR1, GR3 and GR2, GR4 (as from the nomenclature of Ruano et al) would be produced by restriction digestion (as taught in Fig 1 of Rein et al) instead of by a first PCR amplification with GR5 and GR6 (as taught by Fig 1 of Ruano et al). Thus the determined haplotype would include polymorphic markers such as SNPs (determined by PCR as taught by Ruano et al) that are next to (e.g. the polymorphic sites would be adjacent to the cut site determined by the action of an m^5C -requiring restriction enzyme) the methylation site analyzed by the restriction enzyme. With specific regard to claim 14, it would be obvious to create and analyze numerous replicas, including producing 12-18 replicas, to increase the accuracy of the analysis. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., Ins.43-45).

Double Patenting

13. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to

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identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

14. Claims 1-18 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-18 of copending Application No. 10/542,043. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Relevant art not relied upon by the Examiner

15. The following references, as cited in the Notice of References Cited (form 892) accompanying this office action are relevant to the analysis of polymorphisms in single molecules of nucleic acids, but have not been used for the rejection of claims in this office action: Jeffreys et al (1988) *Nucleic Acids Research* Vol .16 No.23, pp.10953-10971; Jeffreys et al (1990) *Cell* Vol.60, pp.473-485.

Conclusion

No claim is allowable. No claim is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Stephen Kapushoc
Art Unit 1634


JULIET C. SWITZER
PRIMARY EXAMINER